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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/26/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/536,880	ONOUE ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 10-13* is/are rejected.

7)☒ Claim(s) *2-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendments filed on November 29, 2006 and January 19, 2007 is acknowledged.

Claims 1-13 are pending in the application.

Restriction

1. Applicant's election with traverse of Group I (claims 1-12) drawn to a peptide composed of at least 23 residues in the reply filed on November 29, 2006 is acknowledged. The traversal is on the ground(s) that the claims of Groups I and II are integrally linked as compounds and method of use. The Applicants argues that compounds and method of use should be examined together. It is a technical relationship that involves the same features, and it is their technical relationship that defines the contributions which each of the Groups taken as a whole makes over the prior art. This is found persuasive because in a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) a product and a process specially adapted for the manufacture of said product; or

(2) a product and a process of use of said product; or

(3) a product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) a process and a apparatus specifically designed for carrying out said process; or

(5) a product, a process specially adapted for the manufacture of the said product and an apparatus specifically designed for carrying out said process. 37 CFR 1.475. Since

Group I is drawn to a product and Group II is drawn to a method of treating or preventing one or more symptoms using the product as in category (2) of 37 CFR 1.475, thus the Restriction is withdrawn in part.

The Applicants elected the peptide species of Claim 7 with traverse. The Applicants further argue that in chemical cases, a specified group of materials which do not necessarily belong to an otherwise class can be claimed together employing "Markush" language. The Markush practice sanctions the claiming together operable substances which could not be defined by generic language but which nevertheless have a community of chemical or physical characteristics. The members of the Markush grouping only possess at least one property in common which is mainly responsible for the function of chemical relationship. The same utility in a generic sense suffices. The examiner cannot determine if this argument is for Restriction or Election of Species. The Examiner is treating this as an argument for Election of Species. However, this is not found persuasive for Election of Species. As provided by MPEP 803.02, in chemical cases recited as "Markush Claims", the following must be met:

The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and
(B)
(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
(B)
(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved. The Applicants have not met both (A) and (B) criteria for the following reason. Claim 3 recites the species HSDAVFTDDYTRLRRQLAVRRYLAAILGRR. Claim 7 recites the species HSDAIFTDSYSRYRRQLAVRRYLAAVLGRR. The two species have divergence in sequences. Thus, Election of Species is deemed proper.

Therefore, Groups I and II are rejoined and Election of Species is maintained. Election of species filed on January 19, 2007 is acknowledged. The election of species

a method of relaxing the bronchial smooth muscle with traverse is acknowledged, however, the Applicants did not point out the errors, thus the election of traverse is treated as "without traverse". A search was conducted for the elected species of claim 7 and was found to be free of prior art. The search was then extended to claims 2-6 and 8-9, and they too were found free of prior art. Search was then extended to the broad Markush and prior art was found for base claim 1. Claims 1-13 have been examined.

Objection-Claims

2. Claim 1 is objected to because of the following informalities: place the word "variable" before "A", "B", "C"..."L", to make the language more clear (i.e., so that the claim language is made clear as to "A", "C", "D", "E", "G", "H", "I", "K" not representative of amino acids). Appropriate correction is required.

Rejection-35 U.S.C. 112, 2nd

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "an amount of at least 50% by weight based on the entire biologically active peptide" is unclear. It is unclear what the "50% by weight" is based upon. It is unclear if the "50% weight" is based upon another agent or just the

weight of the peptide or total weight of everything including the peptide, another agent, and other carriers.

Rejection-35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dong ZX (US Patent # 6242563) in view of Bolin DR (US Patent # 5141924).

9. The instant claims are drawn to a peptide composed of at least 23 residues from the N-terminal of the peptide represented by formula (I) or a pharmaceutically acceptable salt thereof. The claims are further drawn to a pharmaceutical composition or a pharmaceutically acceptable salt thereof in an amount of at least 50% by weight. The claims are also drawn to the pharmaceutical composition and a method for treating or preventing one or more disease or symptoms of relaxing the bronchial smooth muscle.

10. Dong teaches analogues of PACAP as a pharmaceutical composition useful in treating cerebrovascular ischemia, male impotence, motor-neuron disease, neuropathy, pain, depression, anxiety disorder, brain trauma, memory impairments, dementia, cognitive disorder, central nervous system disease, migraine, neurodegenerative diseases, ischemic heart disease, myocardial infarction, fibrosis, restenosis, diabetes mellitus, muscle disease, gastric ulcer, stroke, atherosclerosis, hypertension, septic shock, thrombosis, retina disease, cardiovascular disease, renal failure or cardiac failure or preventing neuronal cell death in a mammal (see abstract and Claims 18-19). Additionally, the reference discloses that the invention is directed to a pharmaceutical composition comprising an effective amount of a peptide of formula (I) as described or pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier (see

column 5, lines 10-14). The reference further teaches a peptide with formula (I): $(R^1R^2)A^1$-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3, wherein A^1 is His, A^2 is Ser, A^3 is Asp, A^4 is Ala, A^5 is Ile or Val, A^6 is Phe, A^7 is Thr, A^8 is Asp or Glu, A^9 is Ser, A^{10} is Tyr, A^{11} is Ser or Thr, A^{12}, A^{14} and A^{15} are each independently Arg or Lys, A^{13} is Tyr, A^{16} is Gln, A^{17} is Leu, A^{18} is Ala, A^{19} is Val, A^{20}, A^{21} are each independently Lys or Arg, A^{22} is Tyr, A^{23} is Leu, A^{24}, A^{25} is Ala, A^{26} is Leu, Ile, Val, or Ala, A^{27} is Val, A^{28} is Gly, A^{31} is Tyr, A^{33} is Gln, Asn, Glu or Asp, A^{35} is Val, Leu, or Ala, A^{37} is Asn, Gln, Asp, Glu or Ala, R^1 and R^2 are each independently selected from the group consisting of H, R^3 is NH_2, etc. This reads on claim1, since claim 1's limitation is that a peptide composed of <u>at least</u> 23 residues from the N-terminal of the peptide. The claim does not recite in amino acids in specific order, just individual residues, thus, any sequence having at least 23 residues having the amino acids in any order reads on claim 1. The reference further teaches that PACAP is a member of a superfamily that already includes several regulatory peptides, e.g., VIP, PHI, PHV, secretin, helodermin, helospectin I and II, glucagons, GIP and GRF (see column 1, lines 18-20). This reads on claims 10-12. Furthermore, the reference teaches that the relaxant action of PACAP in isolated rabbit precontracted aortic rings is 100-fold more potent than VIP (see column 2, lines 37-39). This reads on claim 11. Furthermore, the reference teaches that PACAP relaxes the airway and vascular smooth muscle in guinea-pig, rat and cat lung (see column 2, lines 45-46). The prior art is silent on the amount of weight of peptide or a pharmaceutically acceptable salt thereof in the composition, it is obvious from the

prior art that it needs to be far less than PACAP. The difference between the reference and the instant claims is that the reference does not teach a method of treating or preventing bronchial smooth muscle.

11. However, Bolin DR (# 5141924) teaches that VIP has been found to relax smooth muscle and it is normally present in airway tissues, it has been hypothesized that VIP may be an endogenous mediator of bronchial smooth muscle relaxation (see column 1, lines 63-66).

12. Therefore, it would have been obvious to the ordinary skilled in the art to combine the teachings of Dong et al and Bolin. There is a reasonable expectation of success, since the prior arts teach VIP analogs for treatment of diseases including muscle disorders. Dong et al teach that PACAP relaxes the airway and vascular smooth muscle and Bolin DR teaches that VIP has been found to relax smooth muscle, it would be obvious to try other VIP analogs to treat the same disease and expect similar results.

Allowable Subject Matter

Objection-Claims

13. Claims 2-9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

14. Claims 2-9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the

base claim and any intervening claims. Claims 1 and 10-13 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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